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[REDACTED] EXAMINER

GAMBEL, PHILLIP

ART UNIT	PAPER NUMBER
1644	18

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/816 697	LORENE Z	
	Examiner GAMBER	Art Unit 1644	
- The MAILING DATE of this communication appears on the cover sheet with the correspondence address -			
Period for Reply			
A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>3</u> MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.			
<p>- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.</p> <ul style="list-style-type: none"> - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely. - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). - Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b). 			
Status			
1) <input checked="" type="checkbox"/> Responsive to communication(s) filed on <u>4/8/03</u> 2a) <input checked="" type="checkbox"/> This action is FINAL. 2b) <input type="checkbox"/> This action is non-final. 3) <input type="checkbox"/> Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under <i>Ex parte Quayle</i> , 1935 C.D. 11, 453 O.G. 213.			
Disposition of Claims			
4) <input type="checkbox"/> Claim(s) _____ is/are pending in the application. <u>26-56</u> 4a) Of the above claim(s) _____ is/are withdrawn from consideration. 5) <input type="checkbox"/> Claim(s) _____ is/are allowed. 6) <input type="checkbox"/> Claim(s) _____ is/are rejected. <u>26-56</u> 7) <input type="checkbox"/> Claim(s) _____ is/are objected to. 8) <input type="checkbox"/> Claim(s) _____ are subject to restriction and/or election requirement.			
Application Papers			
9) <input type="checkbox"/> The specification is objected to by the Examiner. 10) <input checked="" type="checkbox"/> The drawing(s) filed on <u>4/8/03</u> is/are: a) <input checked="" type="checkbox"/> accepted or b) <input type="checkbox"/> objected to by the Examiner. Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a). 11) <input type="checkbox"/> The proposed drawing correction filed on _____ is: a) <input type="checkbox"/> approved b) <input type="checkbox"/> disapproved by the Examiner. If approved, corrected drawings are required in reply to this Office action. 12) <input type="checkbox"/> The oath or declaration is objected to by the Examiner.			
Priority under 35 U.S.C. §§ 119 and 120			
13) <input type="checkbox"/> Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). a) <input type="checkbox"/> All b) <input type="checkbox"/> Some * c) <input type="checkbox"/> None of: 1. <input type="checkbox"/> Certified copies of the priority documents have been received. 2. <input type="checkbox"/> Certified copies of the priority documents have been received in Application No. _____. 3. <input type="checkbox"/> Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)). * See the attached detailed Office action for a list of the certified copies not received. 14) <input type="checkbox"/> Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application). a) <input type="checkbox"/> The translation of the foreign language provisional application has been received. 15) <input type="checkbox"/> Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.			
Attachment(s)			
1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.		4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s) _____. 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) 6) <input type="checkbox"/> Other: _____.	

PAPER NO. 18

BEST AVAILABLE COPY

Serial No. 09/816697
Art Unit 1644

DETAILED ACTION

1. Applicant's amendment, filed 4/8/03 (Paper No. 16), has been entered.

Claims 26-32, 44, 45, 47 and 48 have been amended.

Claims 49-56 have been added.

Claims 26-56 are being acted upon presently

Claims 1-25 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.

This Office Action will be in response to applicant's arguments, filed 4/8/03 (Paper No. 16).

The rejections of record can be found in the previous Office Action (Paper No. 14).

3. Formal drawings submitted 4/18/03 (Paper No. 17) comply with 37 CFR 1.84.

4. Applicant's amendment, filed 4/8/03 (Paper No. 16), indicates that a Sequence Listing has been submitted, however no such Sequence Listing appears with applicant's amendment.

Applicant is required to provide the appropriate Sequence Listing to place this application in compliance with the Sequence Rules (see 37 CFR 1.821-1.825).

5. Claims 26-29, 31-35, 37-48 and newly added claims 49-56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection

Applicant's arguments, filed 4/8/03 (Paper No. 16), have been fully considered but are not found convincing essentially for the reasons of record, which are reiterated herein for applicant's convenience.

In asserting that the burden has not shifted to applicant, applicant asserts that the subject matter of the claim need not be described literally in order to meet the written description requirement

Applicant asserts that given the 316 contiguous amino acids in SEQ ID NO: 2, the skilled artisan would recognize that applicant was in possession of the genus of all contiguous sequence that can be derived from SEQ ID NO: 2 because the chemical identity of any species can be immediately envisaged.

Applicant asserts that the disclosure of a full-length amino acid and nucleotide sequence of SLIC-1, a truncated form of SLIC-1 and an assay for determining whether a SLIC-1 protein retains the PSLG-1-binding activity, a skilled artisan could readily envisage multiple species within the genus of variants of SEQ ID NO: 2 that retain PSLG-1 binding activity.

Serial No. 09/816697
Art Unit 1644

Relying upon the Written Description Guidelines Training Materials, applicant asserts that the greater structural details provided instant disclosure satisfies the written description requirement.

Noting entities such as T7, GST, maltose E-binding protein and protein A, applicant asserts that the specification provides sufficient support for sequences associated with SLIC-1

Applicant notes that the specification discloses that amino acids 226-316 of SEQ ID NO: 2 are not required for PSLG-1, whereas amino acids 1-160 are not sufficient for the binding (e.g. see page 75, paragraph 1 of the instant specification). Applicant, in turn, asserts that the skilled artisan would be easily able to determine whether a fragment binds to PSLG-1 binding using the procedures set forth in Example 4.

Here, it is noted that amino acid residues 1-226 of SLIC-1 are capable of mediating the interaction between SLIC-1 and PSLG-1, however amino acids 1-88 and 1-160 fail to mediate the interaction between SLIC-1 and PSLG-1.

However, the claims still recite "SLIC-1" in the absence of a SEQ ID NO. as well reciting limitations that do not encompass critical domain or motifs that read or satisfy the written description of the SLIC-1 protein and fragments thereof rather than the SLIC-1 disclosed as SEQ ID NO: 2 and which binds to PSLG-1.

However, applicant has not provided sufficient written description of the critical residues associated with mediating the interaction between SLIC-1 and PSLG-1. Rather, applicant appears to rely additional procedures to identifying such critical domains or motifs in the amino acids set forth in SEQ ID NO: 2. Again, certain claims are limited to SEQ ID NO:2 but simply rely upon the recitation of SLIC-1 in the absence of the sole sequence disclosed in the specification as filed.

The specification does not provide adequate written description of the claimed invention, for "a SLIC-1 protein" (recited in claims 26-27), "at least 90% identical to SEQ ID NO: 2" (recited in claims 31-33, 39) "comprises" "a sequence" or "at least contiguous amino acids of ... a sequence or a SEQ ID NO" (recited in claims 28-45" and "at least one immunoreceptor tyrosine motif" (recited in claim 46) because the relevant identifying characteristics such as structure or other physical and/or chemical characteristics of said proteins or sequences are not set forth in the specification as-filed, commensurate in scope with claimed invention.

In addition, there does not appear sufficient written description for the elements of claim 40, including (1) a protein comprising a SH2 domain, (2) intracellular domain of PSLG-1, (3) intracellular signaling molecule and (4) a cytoskeletal protein".

Serial No. 09/816697
Art Unit 1644

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Thus, the specification fails to describe these DNA sequences. The Court further elaborated that generic statements are not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function.

Finally, the Court indicated that while applicants are not required to disclose every species encompassed within a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, defined by nucleotide sequence, falling within the scope of the genus, See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicant is claiming a generic class of "SLIC proteins", a generic class of SLIC-1 proteins "comprising fragments" of certain SLIC-1 proteins or a generic class of "tyrosine base motifs" based upon the support of the disclosure of a limited representative number of species (e.g. SEQ ID NO: 1 or 2).

Page 24, paragraph 4 of the instant invention discloses that the claims could encompass a number of natural allelic variants or mutants (e.g. see page 24, paragraph 4). However, it is not appear that the specification as filed provides sufficient written description of the genus of SLIC proteins other than that set forth in SEQ ID NOS: 1 and 2.

Page 24, paragraph 2 discloses that the biological active portions of a SLIC-1 protein is a fragment of SLIC-1 protein which participates in an interaction between a SLIC-1 molecule and a non-SLIC-1 molecule. In addition, this paragraph discloses that the biologically active fragments should contain domains or motifs that modulate signal transduction, PSGL association with the cytoskeleton or cell adhesion. However, it does not appear that the specification as filed has provided sufficient written description of the biologically active fragments (e.g. domains or motifs) that provide the asserted biological functions of SLIC-1 as set forth in SEQ ID NOS: 1 and 2. Again, the specification as filed does not appear to provide written description of natural allelic variants or mutants of the disclosed SLIC-1 proteins and, in turn, the biologically active fragments of said allelic variants and mutants.

Serial No. 09/816697
Art Unit 1644

It is noted that the claims drawn to claims "comprising fragments" do not recite functional language. Even if the claims did recite "biologically active fragments", it is not readily apparent that there is sufficient written description of the SLIC-1 proteins or polypeptides that "comprising at least" "a certain number of amino acids" which correlates to the disclosed functions. Furthermore, these claims recite "comprising" and there does not appear sufficient written description of the additional sequences associated with the claims SLIC-1 proteins or polypeptides that do not contain the entire protein.

In addition, it is noted that page 24, line 27 does not disclose any representative immunoreceptor tyrosine-based activation motif.

The instant specification does not provide sufficient written description as to the critical structural features of said "SLIC proteins""molecules" and the correlation between the chemical structure and the desired structural and/or function.

Applicant is relying upon certain structural and/or biological activities and the disclosure of a limited representative number of species to support entire genuses. The reliance on the disclosed limited examples of SLIC-1 as set forth in SEQ ID NOS: 1 and 2 does not support the written description of any "member" of these claimed SLIC-1 proteins and polypeptides."

Further it does not appear that the specification has provided sufficient written description of a representative number of species for the elements of claim 40, including (1) a protein comprising a SH2 domain, (2) intracellular domain of PSGL-1, (3) intracellular signaling molecule and (4) a cytoskeletal protein".

It has been well known that minor structural differences even among structurally related compounds or compositions can result in substantially different biological or pharmacological activities.

Mere idea or function is insufficient for written description; isolation and characterization at a minimum are required

The instant specification and claims do not provide sufficient functional characteristics coupled with a known or disclosed correlation between function and structure. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus / genuses, and because the genus / genuses is / are highly variable, the disclosure of the particular SLIC-1 proteins set forth in SEQ ID NOS 1 and 2 is insufficient to describe the genus of molecules, encompassed by the claimed invention.

Serial No. 09/816697
Art Unit 1644

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

In the absence of structural characteristics that are shared by members of the genus or genuses of "the claimed SLIC-1 proteins and polypeptides", one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus / genuses. Thus, applicant was not in possession of the claimed genus / genuses. See University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant's arguments are not found persuasive.

6. Claims 26-29, 31-35, 37-48 and newly added claims 49-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "SLIC-1 set forth in SEQ ID NOS: 1 and 2" and , does not reasonably provide enablement for any "SLIC-1 protein or polypeptide" including "at least 90% identical to SEQ ID NO: 2" (recited in claims 31-33, 39) "comprises" "a sequence" or "at least contiguous amino acids of ... a sequence or a SEQ ID NO" (recited in claims 28-45) , encompassed by the claimed invention.

Claims 26-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "inhibiting signal transduction, association with the cytoskeleton or cell adhesion via PSGL-1", does not reasonably provide enablement for any "activity of said SLIC-1 protein", encompassed by the claimed invention.

Applicant's arguments, filed 4/8/03 (Paper No. 16), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant asserts that the burden has not shifted to applicant.

Serial No. 09/816697
Art Unit 1644

Given that the claims are directed to methods of identifying a compound which inhibits / increase binding of a SLIC-1 protein to PSGL-1, applicant asserts that Kuntz is not relevant because the claims of the present invention do not require that the compound which is test be a drug or otherwise a product possess any specific properties.

Given that Skolnick is concerned with predicting a function of a newly discovered gene for which no function is known, applicant asserts that the problem discussed in Skolnick is not applicable to the present disclosure.

Applicant asserts that one does not need to know what the structure is in order to make and use their invention and therefore is not applicable to applicant's invention.

Applicant relying in part upon Fersht (Structure and Mechanism in Protein Science, W.H. Freeman and Company, N.Y. 1998, page 33-34) asserts that a considerable number of species in the claimed genus would retain the function.

Applicant acknowledges that it is well known that even a single point mutation may result in loss of function, but assert that it is commonly observed that a function is retained even when a significant number of amino acids have been deleted or otherwise mutated. Applicant relies upon Example 4 to illustrate that even with one third of all amino acids deleted, the truncated SLIC-1 protein retained the ability to bind PSGL-1.

Applicant argues that the primary structure disclosed in the specification fully satisfies the enablement requirement and that screening methods are routine in the art (e.g. see Ligand-Bind Assays: Labels and Analytical Strategies, Kricka L., Marcel Dekker , Inc. N.Y., 1985, pages 1-3).

Consistent with applicant's acknowledgment that single point mutations may result in the loss of function, amino acid changes can have profound effects on ligand binding, including those molecules associated with adhesion. For example, see Kogan et al. J. Biol. Chem. 270: 14047-14055 (1995); Olivier et al. J. Biol. Chem. 271: 7289-7292 (1996); Insug et al. Peptides 23: 999-1010 (2002).

Here, it is noted that amino acid residues 1-226 of SLIC-1 are capable of mediating the interaction between SLIC-1 and PSGL-1, however amino acids 1-88 and 1-160 fail to mediate the interaction between SLIC-1 and PSGL-1.

However, the claims still recite "SLIC-1" in the absence of a SEQ ID NO. as well reciting limitations that do not encompass critical domain or motifs that read or satisfy the enablement of the claimed SLIC-1 protein and fragments in contrast to the SLIC-1 disclosed as SEQ ID NO: 2 and which binds to PSGL-1.

Serial No. 09/816697
Art Unit 1644

However, applicant has not provided sufficient enablement of the critical residues associated with mediating the interaction between SLIC-1 and PSGL-1. Rather, applicant appears to rely additional procedures to identify such critical domains or motifs in the amino acids set forth in SEQ ID NO: 2. Again, certain claims are limited to SEQ ID NO:2 but simply rely upon the recitation of SLIC-1 in the absence of the sole sequence disclosed in the specification as filed. In contrast to applicant's assertions, there is insufficient direction and guidance as to the critical residues or structures to provide a sufficient number of species to support the claimed invention.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The factors most relevant to this rejection are the scope of the claim, unpredictability in the art, the amount of experimentation required, and the amount of direction or guidance presented.

Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies SLIC-1 proteins and polypeptides that comprise "at least 90% identical to SEQ ID NO: 2" . "comprises" "a sequence" or "at least contiguous amino acids of ... a sequence or a SEQ ID NO".

While "SLIC-1 protein or polypeptide" may have some notion of the structure or activity of these molecules, claiming biochemical molecules by a certain name as well as sequence identity or partial sequences fails to distinctly claim what that molecule is and what it is made up of. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe nor enable any "SLIC-1 protein or polypeptide" including "at least 90% identical to SEQ ID NO: 2" (recited in claims 31-33, 39) "comprises" "a sequence" or "at least contiguous amino acids of ... a sequence or a SEQ ID NO" (recited in claims 28-45"), encompassed by the claimed invention

Applicant is claiming a generic class of "SLIC proteins", a generic class of SLIC-1 proteins "comprising fragments" of certain SLIC-1 proteins or a generic class of "tyrosine base motifs" based upon the support of the disclosure of a limited representative number of species (e.g. SEQ ID NO: 1 or 2).

Page 24, paragraph 4 of the instant invention discloses that the claims could encompass a number of natural allelic variants or mutants (e.g. see page 24, paragraph 4). However, it is not appear that the specification as filed provides sufficient written description of the genus of SLIC proteins other than that set forth in SEQ ID NOS: 1 and 2.

Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality requires a knowledge of and guidance with regard to which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved, and detailed knowledge of the ways in which a polypeptide's structure relates to its functional usefulness. However, the problem of predicting a polypeptide structure from the disclosure of a limited sequence or a limited number of molecules (e.g. SEQ ID NOS: 1 and 2 disclosed in the specification and claimed) and, in turn, utilizing predicted structural determinations to ascertain binding or functional aspects of the claimed SLIC-1 proteins and polypeptides and finally what changes can be tolerated with respect thereto is complex and well outside the realm of routine experimentation. Also, given the partial sequences, there appears insufficient enablement as to what can be added to the partial sequences of SEQ ID NO:1 and 2 that can provide the appropriate functional and structural requirements for SLIC-1 proteins and polypeptides to be employed in the claimed methods.

In re Fisher, 1666 USPQ 19 24 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. It has been well known to those skilled in the art at the time the invention was made that minor structural differences among structurally related compounds or compositions can result in substantially different biological and pharmacological activities.

A person of skill in the art would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences. There is insufficient guidance based on in vitro characterization assays to direct a person of skill in the art to select particular sequences as essential for the characterization of their ability to modulate signal transduction, PSLG association with the cytoskeleton or cell adhesion. A person of skill in the art could not predict which particular amino acid sequences of SEQ ID NOS: 1 and 2 of the disclosed SLIC-1 proteins are essential and could be used in the claimed screening assays.

Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) disclose that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Thus an assignment of function based upon sequence homology or identity without further functional analysis does not appear to provide sufficient enabling support for the claimed Toll homolog encoding nucleic acids and so the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue

Serial No. 09/816697
Art Unit 1644

In further support for the lack of predictability in determining in structure and function Ngo et al. (in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.) disclose that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) was not well understood and was not predictable. Therefore making and using the breadth of molecules in the claimed methods would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, making and using the SLIC-1 proteins and polypeptides comprising "partial sequences of" and/or "sequences at least 90% identical to" SEQ ID NO: 1 while providing or maintaining the claimed specificity and functional characteristics of SEQ ID NOS: 1 and 2 would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Page 24, paragraph 2 discloses that the biological active portions of a SLIC-1 protein is a fragment of SLIC-1 protein which participates in an interaction between a SLIC-1 molecule and a non-SLIC-1 molecule. In addition, this paragraph discloses that the biologically active fragments should contain domains or motifs that modulate signal transduction, PSLG association with the cytoskeleton or cell adhesion. However, it does not appear that the specification as filed has provided sufficient enablement of the activity or the biologically active fragments (e.g. domains or motifs) that provide the asserted biological functions of SLIC-1 as set forth in SEQ ID NOS: 1 and 2.

Further, the specification as filed does not appear to provide enablement of natural allelic variants or mutants of the disclosed SLIC-1 proteins and, in turn, the biologically active fragments of said allelic variants and mutants that would have the same properties of SLIC-1 set forth in SEQ ID NOS: 1 and 2, including the inhibition of signal transduction, association with the cytoskeleton or cell adhesion via PSLG-1.

Applicant has not provided sufficient direction how to make and to use SLIC-1 to screen for any "activity" in order to identify compounds.

Applicant should limit the methods for identifying a compound which inhibits the activity of a SLIC-1 protein to specific and discrete endpoints such as the inhibition of signal transduction, association with the cytoskeleton or cell adhesion via PSLG-1 (or other endpoints enabled by the instant disclosure).

It is noted that the claims drawn to claims "comprising fragments" do not recite functional language. Even if the claims did recite "biologically active fragments", it is not readily apparent that there is sufficient enablement of the SLIC-1 proteins or polypeptides that "comprising at least" "a certain number of amino acids" which correlates to the disclosed functions.

Serial No. 09/816697
Art Unit 1644

The success of state of the art structure-based strategies for inhibitor design is highly unpredictable. For example, Kuntz (Science 257:1078-1082, 1992) on page 1080, column 3, discloses that as little as 2% of compounds predicted to inhibit specific enzymatic or receptor systems actually show inhibition in the micromolar range. Kuntz further discloses that "optimization" of these compounds has proven even more problematic. Therefore, in view of the unpredictability in the art, and in view of the insufficient guidance and working examples in the specification, the quantity of experimentation required by one skilled in the art to practice the invention undue.

The specification does not adequately teach how to effectively identifying a compound which inhibits "any activity" of a SLIC-1 protein including the lack of clear endpoints and the use of variants other than the SLIC-1 proteins set forth in SEQ ID NOS: 1 and 2.

Given the relative incomplete understanding in the biotechnological field involved, and the lack of a reasonable correlation between the narrow disclosure in the specification and the broad scope of protection sought in the claims, a rejection under 35 USC 112, first paragraph for lack of enablement is deemed appropriate.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the modifications in SLIC-1 proteins and the lack of discrete and measurable endpoints, methods of identifying a compound which the activity of a SLIC-1 protein as claimed is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue

Applicant is invited to amend the claims to recite specific and measurable endpoints as well as to limit the SLIC-1 proteins to SEQ ID NOS:1 and 2.

9. Claims 40-43 and 46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

Given the absence of additional arguments in applicant's amendment, filed 4/8/03 (Paper No. 16), this rejection is maintained essentially for the reasons of record and reiterated for applicant's convenience.

The specification does not provide a sufficient enabling description of the claimed invention as it reads on "at least on immunoreceptor tyrosine based motif".

It is noted that page 24, line 27 does not disclose any representative immunoreceptor tyrosine-based activation motif.

Further, it does not appear that the specification has provided sufficient enablement for a representative number of species for the elements of claim 40, including (1) a protein comprising a SH2 domain, (2) intracellular domain of PSGL-1, (3) intracellular signaling molecule and (4) a cytoskeletal protein".

Serial No. 09/816697

Art Unit 1644

A person of skill in the art is not enabled to make and use "at least one immunoreceptor tyrosine based motif" nor the elements of claim 40, as recited in the claims. A person of skill in the art would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences. A person of skill in the art could not predict which particular amino acid sequences of "at least one immunoreceptor tyrosine based motif" are essential and could be used in the claimed screening assays.

"It is not sufficient to define the recombinant molecule by its principal biological activity, e.g. having protein A activity, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property." Colbert v. Lofdahl, 21 USPQ2d, 1068, 1071 (BPAI 1992).

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, making and using use "at least one immunoreceptor tyrosine based motif" or the elements of claim 40 to be employed in the claimed screening methods would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

7. Given applicant's amended claims filed 4/18/03 (Paper No. 16), the previous rejection under 35 U.S.C. § 112, second paragraph, has been withdrawn.

8. No claim is allowed.

It appears that the SLIC-1 protein set forth in SEQ ID NOS: 1 and 2 are free of the art. Accordingly, methods that are drawn to methods of identifying a compound which inhibits the activity of a SLIC-1 protein are free of the art.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Serial No. 09/816697

Art Unit 1644

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gabel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gabel

Phillip Gabel, PhD.

Primary Examiner

Technology Center 1600

June 6, 2003